

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended) ~~Product of the A biochip type,~~  
~~comprising:~~

a flat solid support having a surface covered with a metal capable of coordination bonding with a phosphate group[[,]]; and

at least one biopolymer carrying a free phosphate group  $\text{OP(O)(OH)}_2$  being immobilized on said surface by ionocovalent bonding between the free phosphate group of the polymer and the metal.

2. (currently amended) ~~Product~~ The biochip according to claim 1, wherein the biopolymer is a nucleic acid phosphorylated in the 5' position.

**out** ③ (currently amended) ~~Product~~ The biochip according to claim 1, wherein the biopolymer is a nucleic acid phosphorylated in the 3' position.

4. (currently amended) ~~Product~~ The biochip according to claim 2, characterized in that the nucleic acid has a

~~polyguanine (polyG) spacer group between the body of the nucleic acid and the phosphate group.~~

~~out~~ 5 (currently amended) Product The biochip according to claim 1, wherein the biopolymer is a phosphorylated protein.

~~out~~ 6 (currently amended) Product The biochip according to claim 1, wherein the biopolymer is a phosphorylated oligo- or poly-saccharide.

~~7.~~ (currently amended) Product The biochip according to claim 1, wherein the metal is bound to the surface of the support by way of a spacer molecule.

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pe busha.*

5/14  
polyG

nt(6)



~~8.~~ (currently amended) Product The biochip according to claim 7, wherein the spacer molecule comprises a fatty acid chain carrying a phosphonate group to which the metal binds by ionocovalent bonding.

9. (currently amended) Product The biochip according to claim 1, wherein the metal is zirconium.

10. (currently amended) Product The biochip according to claim 8, wherein the spacer molecule is octadecylphosphonic acid and the metal is zirconium.

11. (currently amended) ~~Product~~ The biochip according to claim 1, wherein the support is glass.

12. (currently amended) ~~Product~~ The biochip according to claim 1, further comprising:

a sheet of glass having a surface covered with a monolayer of zirconium octadecylphosphonate[,]; and

at least one nucleic acid carrying a phosphate group in the 5' position being immobilized on said surface by ionocovalent bonding between the phosphate group of the nucleic acid and the zirconium.

13. (currently amended) Method for making a ~~product~~ of the biochip type, as defined in claim 1, comprising the immobilization of immobilizing at least one biopolymer carrying a free phosphate group on a solid support having a surface covered with a metal capable of coordination bonding with a phosphate group, the biopolymer being immobilized on said surface by ionocovalent bonding between the free phosphate group of the polymer and the metal.

14. (currently amended) Method according to claim 13, also further comprising a step of obtaining the biopolymer carrying a phosphate group.

15. (original) Method according to claim 14, wherein the polymer is a nucleic acid phosphorylated enzymatically in the 5' position.

16. (currently amended) Kit for the preparation of a ~~product of the biochip type~~ as defined in claim 1, comprising the following elements:

- a solid support having a surface covered with a metal capable of coordination bonding with a phosphate group;
- at least one biopolymer carrying a phosphate group;
- optionally reagents.

~~Out~~ 17. (currently amended) Use of a ~~product of the biochip type as defined in claim 1, for the purpose of A method of screening compounds,~~ comprising contacting the biochip of claim 1 with an extract from a biological sample, wherein the extract comprises a compound capable of binding to the immobilized biopolymer of the biochip of claim 1.

~~Out~~ 18. (currently amended) Use of a ~~product of A method of conducting an in vitro diagnosis,~~ comprising conducting said diagnosis with the ~~biochip type~~ as defined in claim 1, as an in vitro diagnostic tool.

19. (currently amended) ~~Product~~ The biochip according to claim 3, characterized in that the nucleic acid has a polyguanine (polyG) spacer group between the body of the nucleic acid and the phosphate group.

Draft I

01 Aug 2007

### **Detailed Action**

#### **Status of Claims**

1. Claims 1-19 are pending in this application. Claims 13-15, 17-18 are withdrawn from consideration. Claims 13-15, 17-18 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election was made with traverse in the reply filed on 07 March 2007.

#### **Election Restriction**

2. Applicants' election of Group I, claims 1-12, 16 and 19, with traverse in the reply filed 7 March 2007, is acknowledged. Applicants' election of the following species is acknowledged.

In claims 1 and 2, applicants elect the species biopolymer as a nucleic acid phosphorylated in the 5' position and a nucleic acid phosphorylated in the 3' position. However, this election is non-compliant with the election of species requirement.

In claim 4, the applicants elect the species of poly G spacer.

During a telephone conversation with Robert Madsen, attorney of record on 26 July 2007 an election of species was made with traverse. The applicants elected the species of nucleic acid phosphorylated in the 5' position as defined by claim 2. Affirmation of this election must be made by applicant in replying to this Office action.

Claims 13-15, 17-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The applicants' arguments regarding the restriction requirement between Groups I and II are found to be persuasive. Therefore, the restriction requirement between groups I and II is withdrawn. However, the Examiner does not persuaded by the applicants' arguments for the use of the kit in claim 16. The Examiner contends that a kit for use in a micro-array experiment exists; and therefore, the inventive and linking concept is not present in the instant case. The restriction is deemed proper and made final.

Claims 3, 5-6, 8, 10 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species and inventions.

Claims 1-2, 4, 7, 9-15, 17-19 are examined.

#### **Claim Rejections – 35 USC § 112**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. For claims 1 and 13, the biopolymer carrying a free phosphate group being immobilized on said surface by ionocovalent bonding between the free phosphate group of the polymer and the metal. The Examiner is unclear how the phosphate group of the nucleic acid can be free and bound to a metal. Therefore claims 1, 13 and all dependent claims are rejected.

### **Claim Rejections – 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. **Claims 1, 7, 9-15, 17-19** are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al, WO 2003/046508 A2 (5 June 2003) in view of Petruska, et al, Thin Solid Films, 327-329 (1998) 131-135, Elsevier Science.

**For claims 1, 7, 9-15, 17-19,** a biochip, comprising a flat solid support having a surface covered with a metal and capable of coordination bonding with a phosphate at least one biopolymer carrying a free phosphate group being immobilized on said surface by ionocovalent bonding between the free phosphate group of the polymer and the metal.

Agrawal et al teach (see paragraph 25) a biomolecule, which can be a nucleic acid, immobilized to a glass solid support substrate (see paragraphs 20 and 80). The biomolecule is covalently/coordinateately attached to the substrate (see paragraphs 131 and 132). The solid support can be coated with an activating material such as zirconia (see paragraphs 42, 144). The activating material is used to help immobilize the biomolecule to the solid support.

The prior art teachings of Agrawal et al differ from the claimed invention as follows:  
Agrawal; et al, fail to teach the following:

*The zirconium*  
Agrawal et al, fail to teach ~~a metal, zirconium~~ is bound to a surface via a support molecule, octadecylphosphonic acid.

However, the teachings of Petruska, et al remedies the deficiencies of Agrawal as follows:

For claim 7, Petruska et al teach (see Scheme 1 and Scheme 2) the biochip according to claim 1, wherein the metal is bound to the surface of the support by way of a spacer molecule.

For claim 10, Petruska et al teach (see abstract, introduction, scheme 2) the biochip according to claim 8, wherein the spacer molecule (also called a capping molecule) is octadecylphosphonic acid and the metal is zirconium.

For claim 12, Petruska et al, teach (see abstract, and definition of Langmuir monolayer method) the biochip according to claim 1, further comprising a sheet of glass having a surface covered with a monolayer of zirconium octadecylphosphonate.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the device and method of immobilizing a nucleic acid on a biochip as taught by Agrawal et al with the Langmuir-Blodgett film method (a Langmuir-Blodgett (LB) film is a set of monolayers, or layers of organic material one molecule thick, deposited on a solid substrate. An LB film can consist of a single layer or many) as taught by Petruska.

Petruska teaches

A person of ordinary skill in the art would have been motivated to combine the device of the biochip and the method of making the biochip because the Langmuir-Blodgett method because the zirconium/phosphate interaction is strong, and the nature of the stepwise procedure employed allows for the easy construction of alternating layer of LB films which results in a procedure that is an extremely convenient way to prepare alternating layer films (see introduction, Petruska, et al). Furthermore, because of the strength of the metal-head group interactions, zirconium phosphate films are extremely stable LB assemblies (see conclusions, Petruska et al).

Finally a person of ordinary skill in the art would have had a reasonable expectation of success because utilizing the system described by Petruska to more stably immobilize a biopolymer to a solid support is a well-known method in the art. The Langmuir-Blodgett method is well described in the prior art and has robust elements for reliably coordinately bonding a metal to an organic molecule on a solid support.

5. Claims 2, 4 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al, WO 2003/046508 A2 (5 June 2003) in view of Petruska, et al, Thin Solid Films, 327-329 (1998) 131-135, Elsevier Science as applied to claims 1, 7, 9-15, 17-19 above, and further in view of Gagna et al, US Patent 6,936,461 (Date of Patent 30 August 2005)

Agrawal et al, in view of Petruska et al, fail to teach a nucleic acid phosphorylated in the 5' position and polyG spacer group.

However, the teachings of Gagna et al remedies the deficiencies of Agrawal et al, in view of Petruska et al, as follows:

For claims 2, 4 and 19 the biochip according to claim 1, wherein the biopolymer is a nucleic acid phosphorylated in the 5' position; furthermore, the nucleic acid has a polyguanine spacer group between the nucleic acid and the phosphate group

Gagna et al teach (see column 17, line 66, column 23, line 58) a nucleic acid phosphorylated in the 5' position. Each nucleic acid has a tail (which the examiner contends is a linker or spacer) to help immobilize the nucleic acid to the substrate (see column 25, lines 33-37).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine and modify the teachings of a biochip containing a nucleic acid immobilized on a solid support and the method of making the biochip as taught by Agrawal et al., and the method of coating a glass solid support with the metal Zirconium covalently attached to a phosphate group as taught by Petruska et al with linker attached to the body of a nucleic acid phosphorylated in the 5' position as taught by Gagna et al.

A person of ordinary skill in the art would have been motivated to combine and modify the teachings of Agrawal et al, in view of Petruska et al, to include the use of a linker attached to the body of a nucleic acid phosphorylated in the 5' position as taught by Gagna et al because the tail or linker immobilizes the nucleic acid more firmly to the substrate (see column 25, lines 33-37). Also, by attaching the nucleic acid to the glass surface allows the investigator the ability to characterize nucleic acid/probe interactions (see column 23, lines 24-26).

Finally a person of ordinary skill in the art would have had a reasonable expectation of success because the methods of using modified nucleic acids attached to a solid support as taught by Gagna et al, is well known in the art for use in this manner.

### **Conclusion**

6. Claims 1-2, 4, 7, 9-15, 17-19 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Garrison Owens whose telephone number is 571-270-3060. The examiner can normally be reached on Monday - Thursday, 7:30AM - 5:PM, ALT. Wednesday.,

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571-272-0763. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

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